

Application No. 09/701,463  
Amendment dated August 11, 2003  
Page 2

**Amendments to the Claims:**

The following claims will replace all prior versions of the claims in this application (in the unlikely event that no claims follow herein, the previously pending claims will remain):

1-30. (Cancelled).

---

*CJ*

31. (Currently amended) A pharmaceutical composition comprising: A pharmaceutically acceptable carrier, diluent or excipient; and a biologically active lipid mobilizing agent for use in therapy

which wherein said lipid mobilizing agent has an apparent molecular mass  $M_r$  as determined by gel exclusion chromatography greater than 6.0 kDa, which is capable of inducing lipolysis in mammalian adipocytes, and which has the properties and characteristics of a Zn- $\alpha_2$ -glycoprotein.

32. (Currently amended) The pharmaceutical composition of claim 31 wherein said A purified biologically active lipid mobilizing agent as claimed in claim 31 for use in therapy which is substantially free of proteolytic activity and which consists essentially of a glycosylated polypeptide having an apparent relative molecular mass  $M_r$  of about 43 kDa as determined by its electrophoretic mobility when subjected to 15% SDS-PAGE electrophoresis and having homology in amino acid sequence with the amino acid sequence (SEQ ID No: 1) of human plasma Zn- $\alpha_2$ -glycoprotein.

33. (Currently amended) The pharmaceutical composition of claim 32 wherein said A lipid mobilizing agent as claimed in claim 32 which is obtainable by a process that includes sequential steps of subjecting biological material to ion exchange chromatography, exclusion chromatography, and then to hydrophobic interaction chromatography, said biological material being urine from a cancer cachexia patient or an extract of a culture of a MAC16 tumor cell line deposited under the provisions of the Budapest Treaty in the European Collection of Animal Cell Cultures (ECACC) under an Accession No. 89030816.

Application No. 09/701,463  
Amendment dated August 11, 2003  
Page 3

34. (Currently Amended) The pharmaceutical composition of claim 31 wherein said A biologically active lipid mobilizing agent ~~as claimed in claim 31 for therapeutic use which is a glycosylated polypeptide wherein the polypeptide moiety is selected from one of the following groups:~~

- (a) a polypeptide having the amino acid sequence of a Zn- $\alpha_2$ -glycoprotein;
- (b) a polypeptide which in respect to (a) is deficient in one or more amino acids that do not significantly affect the lipid mobilizing the lipolytic activity;
- (c) a polypeptide in which in respect to (a) one or more amino acids are replaced by a different amino acid or acids that do not significantly affect the lipid mobilizing or lipolytic activity;
- (d) a polypeptide in which in respect to (a) there is incorporated a plurality of additional amino acids which do not interfere with the biological lipolytic activity.

35. (Currently amended) The pharmaceutical composition of claim 31 wherein said A biologically active lipid mobilizing agent ~~for use in therapy as claimed in claim 31 consisting essentially of includes~~ a glycoprotein that has a polypeptide amino acid sequence homologous with the amino acid sequence (SEQ ID No: 1) of human plasma Zn- $\alpha_2$ -glycoprotein, or with a variant thereof which is modified by minor additions, deletions, or substitutions that do not substantially affect its lipid mobilizing activity in biological systems.

36. (Currently amended) The pharmaceutical composition of claims 34 wherein said A lipid mobilizing agent ~~for use in therapy as claimed in claim 34 or 35 further characterized in that it has having~~ an apparent relative molecular mass M, of about 43 kDa as determined by its electrophoretic mobility when subjected to 15% SDS-PAGE electrophoresis.

37. (Currently amended) The pharmaceutical composition of claim 31 wherein said A lipid mobilizing agent ~~for use in therapy as claimed in claim 31 wherein its loses~~ lipid mobilizing properties ~~are destroyed~~ when subjected to digestion with chymotrypsin.

Application No. 09/701,463  
Amendment dated August 11, 2003  
Page 4

38. (Currently amended) The pharmaceutical composition of claim 31 wherein said A lipid mobilizing agent for use in therapy as claimed in claim 31 wherein it has the potential *in vitro* to stimulate adenylate cyclase activity in a guanine triphosphate (GTP) dependent process upon incubation with murine dipocyte plasma membranes.

39. (Currently amended) The pharmaceutical composition of claim 31 wherein said A lipid mobilizing agent for use in therapy as claimed in claim 31 which has substantially the same immunological properties as human Zn- $\alpha_2$ -glycoprotein.

*C2*  
*Agmt/*

40. (Currently amended) The pharmaceutical composition of claim 31 wherein said A biologically active lipid mobilizing agent for use in therapy which is capable of inducing lipolysis in mammalian adipocytes characterized, which has an apparent molecular mass M<sub>r</sub> as determined by gel exclusion chromatograph greater than 6.0 kDa, and which is obtainable is obtained by subjecting the lipid mobilizing agent claimed in claim 31 to fragmentation by enzymatic degradation.

41. (Currently amended) The pharmaceutical composition of claim 40 wherein said A biologically active lipid mobilizing agent as claimed in claim 40 for use in therapy that is a fragment of a glycoprotein or glycosylated polypeptide which is a component of the lipid mobilizing agent claimed in claim 31 produced by digesting the latter with trypsin.

42. (Currently amended) The pharmaceutical composition of claim 31 wherein said A lipid mobilizing agent for use in therapy as claimed in claim 31 which is substantially free of proteolytic activity.

43. (Currently amended) The pharmaceutical composition of claim 31 wherein said A lipid mobilizing agent comprises for use in therapy as claimed in claim 31 wherein the a polypeptide chain of the polypeptide component has having an N-terminus blocked by a pyroglutamate residue.

Application No. 09/701,463  
Amendment dated August 11, 2003  
Page 5

44. (Currently amended) The pharmaceutical composition of claim 31 wherein the lipid mobilizing activity of said A lipid mobilizing agent for use in therapy as claimed in claim 31 wherein the lipid mobilizing activity is destroyed by periodate treatment.

*C1*  
*Cancelled*

45. (Currently amended) A method of isolating and purifying a lipid mobilizing agent having the properties and characteristics of a Zn- $\alpha_2$ -glycoprotein, said method comprising: subjecting an extract of a cachexia-inducing tumor or of a culture of a cachexia-inducing tumor cell line, or a sample of urine or other body fluid of a mammal bearing a cachexia-inducing tumor, to a combination of ion exchange, gel filtration size exclusion chromatography, and hydrophobic interaction chromatography, and recovering a single product or molecular species having an apparent relative molecular mass of 43 kDa, as determined by 15% SDS-PAGE electrophoresis, which is substantially free of proteolytic activity.

46. (Cancelled)

*C2*

47. (Currently amended) A pharmaceutical composition as claimed in claim 46 31 which is an injectable formulation incorporating a carrier in the form of a pharmaceutically acceptable injection vehicle.

48. (Previously added) A method of treating a mammal to bring about a weight reduction or reduction in obesity, said method comprising administering to the mammal in need of such treatment a therapeutically effective dosage of a lipid mobilizing agent as claimed in claim 31.

Application No. 09/701,463  
Amendment dated August 11, 2003  
Page 6

OB

49. (Currently amended) A method of treating a mammal to bring about a weight reduction or reduction in obesity, said method comprising administering to the mammal in need of such treatment a therapeutically effective dosage of a glycoprotein identical to or homologous with human Zn- $\alpha_2$ -glycoprotein, or an effective lipolytically active fragment thereof which has an apparent molecular mass  $M_r$  as determined by gel exclusion chromatography that is greater than 6.0 kDa, substantially free of any proteolytic proteolytic activity.

50-59. (Cancelled).